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LOGINID: SSSPTA1623PAZ

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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* * * * * * * *
                    Welcome to STN International
                Web Page URLs for STN Seminar Schedule - N. America
NEWS 1
                "Ask CAS" for self-help around the clock
NEWS 2
                CA/CAplus records now contain indexing from 1907 to the
NEWS 3
        SEP 09
                present
NEWS 4 DEC 08 INPADOC: Legal Status data reloaded
NEWS 5 SEP 29 DISSABS now available on STN
NEWS 6 OCT 10 PCTFULL: Two new display fields added
NEWS 7 OCT 21 BIOSIS file reloaded and enhanced
NEWS 8 OCT 28 BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 9 NOV 24 MSDS-CCOHS file reloaded
NEWS 10 DEC 08 CABA reloaded with left truncation
NEWS 11 DEC 08 IMS file names changed
NEWS 12 DEC 09 Experimental property data collected by CAS now available
                 in REGISTRY
                STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 13 DEC 09
                DGENE: Two new display fields added
NEWS 14 DEC 17
                BIOTECHNO no longer updated
NEWS 15 DEC 18
                CROPU no longer updated; subscriber discount no longer
NEWS 16 DEC 19
                 available
NEWS 17 DEC 22 Additional INPI reactions and pre-1907 documents added to CAS
                 databases
                IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 18 DEC 22
NEWS 19 DEC 22 ABI-INFORM now available on STN
NEWS 20 JAN 27 Source of Registration (SR) information in REGISTRY updated
                 and searchable
NEWS 21 JAN 27 A new search aid, the Company Name Thesaurus, available in
                 CA/CAplus
                 German (DE) application and patent publication number format
NEWS 22 FEB 05
                 changes
NEWS 23 MAR 03 MEDLINE and LMEDLINE reloaded
NEWS 24 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 25 MAR 03 FRANCEPAT now available on STN
NEWS EXPRESS MARCH 5 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
              MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004
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=> file reg COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

0.21 0.21

FILE 'REGISTRY' ENTERED AT 06:56:57 ON 16 MAR 2004 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2004 American Chemical Society (ACS)

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15 MAR 2004 HIGHEST RN 663595-21-9 STRUCTURE FILE UPDATES: DICTIONARY FILE UPDATES: 15 MAR 2004 HIGHEST RN 663595-21-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> logoff hold COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

0.63

0.42

FULL ESTIMATED COST

SESSION WILL BE HELD FOR 60 MINUTES STN INTERNATIONAL SESSION SUSPENDED AT 06:57:03 ON 16 MAR 2004

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LOGINID: SSSPTA1623PAZ

PASSWORD:

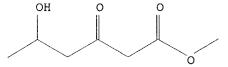
* * * * * RECONNECTED TO STN INTERNATIONAL * * * * * SESSION RESUMED IN FILE 'REGISTRY' AT 07:17:33 ON 16 MAR 2004 FILE 'REGISTRY' ENTERED AT 07:17:33 ON 16 MAR 2004 COPYRIGHT (C) 2004 American Chemical Society (ACS)

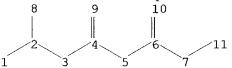
SINCE FILE TOTAL COST IN U.S. DOLLARS ENTRY SESSION 0.63 0.42

FULL ESTIMATED COST

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Uploading C:\Examination Auxillary files\10705665\10705665 product.str





chain nodes :

1 2 3 4 5 6 7 8 9 10 11

chain bonds :

1-2 2-3 2-8 3-4 4-5 4-9 5-6 6-7 6-10 7-11

exact/norm bonds :

2-8 4-9 6-7 6-10 7-11

exact bonds:

1-2 2-3 3-4 4-5 5-6

Match level:

1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS

10:CLASS 11:CLASS

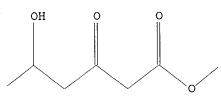
L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS

L1

STR



Structure attributes must be viewed using STN Express query preparation.

=> logoff hold

COST IN U.S. DOLLARS

SINCE FILE

LATOT

FULL ESTIMATED COST

ENTRY SESSION 0.42 0.63

SESSION WILL BE HELD FOR 60 MINUTES STN INTERNATIONAL SESSION SUSPENDED AT 07:18:11 ON 16 MAR 2004

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PASSWORD:

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COPYRIGHT (C) 2004 American Chemical Society (ACS)
                                                                TOTAL
                                                 SINCE FILE
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FULL ESTIMATED COST
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100.0% PROCESSED 98977 ITERATIONS
                                                            1274 ANSWERS
SEARCH TIME: 00.00.02
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=> e tert-butyl acetate/cn
                  TERT-BUTYL 9-TRIPTYCYLCARBONYL PEROXIDE/CN
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            1
                  TERT-BUTYL ABIETATE/CN
E2
            1 --> TERT-BUTYL ACETATE/CN
E3
                  TERT-BUTYL ACETATE RADICAL CATION/CN
E4
            1
                   TERT-BUTYL ACETATE, MONOPROTONATED/CN
E5
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                   TERT-BUTYL ACETATE-D3/CN
            1
E6
                   TERT-BUTYL ACETOACETATE/CN
           1
E7
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                  TERT-BUTYL ACETOACETATE N, N-DIMETHYLHYDRAZONE/CN
E9
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                  TERT-BUTYL ACETOXYACETATE/CN
E11
                   TERT-BUTYL ACETOXYPERACETATE/CN
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E12
=> e3
            1 "TERT-BUTYL ACETATE"/CN
T.3
=> d 13
    ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
     540-88-5 REGISTRY
    Acetic acid, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
    Acetic acid, tert-butyl ester (8CI)
     tert-Butyl alcohol, acetate (6CI)
OTHER NAMES:
    1,1-Dimethylethyl acetate
     Acetic acid tert-butyl ester
CN
     NSC 59719
CN
CN
     TBAc
CN
     tert-Butyl acetate
CN
     Texaco lead appreciator
     3D CONCORD
FS
     C6 H12 O2
MF
CI
     COM
     STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, CA, CAOLD,
T.C.
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CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DETHERM*, DIPPR*, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*,

SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USPAT2, USPATFULL (*File contains numerically searchable property data)

(**Enter CHEMLIST File for up-to-date regulatory information)

Other Sources: DSL**, EINECS**, TSCA**

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1519 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1521 REFERENCES IN FILE CAPLUS (1907 TO DATE)
54 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 165.82 166.03

FULL ESTIMATED COST

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FILE COVERS 1907 - 16 Mar 2004 VOL 140 ISS 12 FILE LAST UPDATED: 15 Mar 2004 (20040315/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> 12 L4 535 L2

=> 13

L5 1521 L3

=> 14 and 15

L6 65 L4 AND L5

=> magnesium

399618 MAGNESIUM

88 MAGNESIUMS

L7 399652 MAGNESIUM

(MAGNESIUM OR MAGNESIUMS)

=> mg

1279869 MG

1213 MGS

L8 1280656 MG

(MG OR MGS)

=> ;17 and 16

L9 6 L7 AND L6

=> 17 and 16

L10 6 L7 AND L6

- L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Chemoenzymatic synthesis of optically active β, δ -dihydroxy esters
- L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
- Process for preparing optically active 2-[6-(hydroxymethyl)-1,3-dioxan-4-yl]acetic acid derivatives as pharmaceutical intermediates
- L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Processes for the preparation of 5-hydroxy-3-oxopentanoic acid derivatives
- L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Process for the preparation of optically active 2-[6-(hydroxymethyl)-1,3-dioxan-4-yl]acetic acid derivatives
- L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Isoquinolone derivatives, their production and use
- L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
- Preparation of anticholesteremic $(R-(R*R*))-2-(4-fluorophenyl)-\beta$, δ -dihydroxy-5-(1-methylethyl-3-phenyl-4((phenylamino)carbonyl)-1H-pyrrolyl-1-heptanoic acid, its lactone form and salts thereof

=> d 110 1-6 ti fbib abs

- L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Chemoenzymatic synthesis of optically active β , δ -dihydroxy esters
- AN 2002:948073 CAPLUS
- DN 138:368633
- TI Chemoenzymatic synthesis of optically active $\beta, \delta\text{-dihydroxy}$ esters
- AU Wolberg, Michael
- CS Germany
- SO Berichte des Forschungszentrums Juelich (2002), Juel-3988, i-xv,1-138 CODEN: FJBEE5; ISSN: 0944-2952
- DT Report
- LA German
- A new access to optically active β, δ -dihydroxy esters and AB δ -hydroxy- β -keto esters is presented. These compds. are valuable intermediates for the synthesis of important natural products and pharmaceuticals, e.g. HMG-CoA reductase inhibitors of the mevinic acid type. The synthesis strategy is based on an unprecedented highly regioand enantioselective biocatalytic reduction of achiral β , δ -diketo esters. In a screening, two enantio-complementary biocatalysts were found to be particularly suitable for this purpose. Thus, the β , δ -diketo ester tert-Bu 6-chloro-3, 5-dioxohexanoate was reduced by NADP(H)-dependent alc. dehydrogenase of Lactobacillus brevis to afford enantiomerically pure δ -hydroxy- β -keto ester tert-Bu (S)-6-chloro-5-hydroxy-3-oxohexanoate in a 72-84% isolated yield (>99.5% ee). The enzyme is readily available in the form of a crude cell extract from a recombinant E. coli strain (recLBADH). A scale-up of the one-step substrate synthesis (140 q scale) and of the enzymic reduction (70 g scale, substrate-coupled NADPH-regeneration) was established. The enantiomeric δ-hydroxy-β-keto ester tert-Bu (R)-6-chloro-5-hydroxy-3oxohexanoate was obtained by reduction of tert-Bu 6-chloro-3,5-dioxohexanoate with Baker's yeast (Saccharomyces cerevisiae). A detailed investigation of the reaction parameters of this whole-cell transformation led to the application of a biphasic system by which the enantiomeric excess could be

raised from 48% ee to 94% ee (50% isolated yield). The β -keto group of both enantiomers thus obtained was reduced by syn- and anti-selective borohydride redns. Combination of the reduction methods afforded all four stereoisomers of the crystalline β, δ -dihydroxy ester tert-Bu 6-chloro-3,5-dihydroxyhexanoate (>99% ee and dr > 200:1 each, 52-70% isolated yield). Alternatively, the syn-(3R,5S)-isomer of this known building block was obtained in one step and with high stereoisomeric purity by reduction of tert-Bu 6-chloro-3,5-dioxohexanoate with whole cells of Lactobacillus kefir. An iodide and an epoxide suitable for C-C-bond formation at C-6 were derived from tert-Bu syn-(3R,5S)-6-chloro-3,5dihydroxyhexanoate. RecLBADH accepts a variety of β , δ -diketo esters as was determined in a photometric assay. The eta, δ -diketo esters tert-Bu 3,5-dioxohexanoate and tert-Bu 3,5-dioxoheptanoate were reduced on a 1-10 mmol scale to afford the corresponding (R)- δ -hydroxy- β -keto esters with 99.4% ee and 98.1% ee, resp. (61-77% isolated yield). The reduction of the branched $\beta, \delta\text{-diketo}$ ester tert-Bu rac-4-methyl-3,5-dioxohexanoate proceeds via a dynamic kinetic resolution which resulted in a 66% isolated yield of the corresponding syn-(4S,5R)-δ-hydroxy-β-keto ester (99.2% ee, dr = 35:1). To underline the applicability of the virtually enantiopure enzymic products, they were used as starting materials for several new natural product syntheses. Furthermore, a convenient process for the large-scale separation of noncrystg. diastereomeric syn- and anti-1,3-diols was developed. The crucial step of this new method is a diastereomerdifferentiating hydrolysis of the resp. acetonides.

RE.CNT 293 THERE ARE 293 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
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- TI Process for preparing optically active 2-[6-(hydroxymethyl)-1,3-dioxan-4-yl]acetic acid derivatives as pharmaceutical intermediates
- AN 2001:904153 CAPLUS
- DN 136:37613
- Process for preparing optically active 2-[6-(hydroxymethyl)-1,3-dioxan-4-yl]acetic acid derivatives as pharmaceutical intermediates
- IN Nishiyama, Akira; Horikawa, Miho; Yasohara, Yoshihiko; Ueyama, Noboru;
 Inoue, Kenji
- PA Kaneka Corporation, Japan
- SO PCT Int. Appl., 107 pp. CODEN: PIXXD2
- DT Patent
- LA Japanese
- FAN.CNT 1

ran.	PATENT NO.	KIND DATE	APPLICATION NO. DATE
PΙ	WO 2001094337	A1 20011213	WO 2001-JP4729 20010605
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			JP 2000-168285 A 20000605
	AU 2001062692	A5 20011217	AU 2001-62692 20010605
			JP 2000-168285 A 20000605
			WO 2001-JP4729 W 20010605
	SI 20874	C 20021031	SI 2001-20003 20010605
			JP 2000-168285 A 20000605
			WO 2001-JP4729 W 20010605
	EP 1288213	A1 20030305	EP 2001-936850 20010605

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                                               JP 2000-168285 A 20000605
                                               WO 2001-JP4729 W 20010605
     CASREACT 136:37613; MARPAT 136:37613
     This document discloses a process for preparing optically active
     2-[6-(hydroxymethyl)-1,3-dioxan-4-yl]acetic acid derivs. which comprises
     reacting an enolate prepared by reacting an acetic acid ester derivative with a
     base or a zero-valent metal with (S)-\beta-hydroxy-\gamma-butyrolactone
     at a temperature of -30°C or above to thereby obtain a
     dihydroxyoxohexanoic acid derivative, treating this derivative with an
acylating
     agent in the presence of a base to thereby obtain a monoacylated derivative of
     dihydroxyoxohexanoic acid, reducing the monoacylated derivative with a
     microorganism into a monoacylated derivative of trihydroxyhexanoic acid,
     treating the resulting derivative with an acetal-forming reactant in the
     presence of an acid catalyst to thereby obtain an
     acyloxymethyldioxanylacetic acid derivative, and subjecting this derivative to
     solvolysis in the presence of a base. The title compds. are intermediates
     for HMG-CoA reductase inhibitors. The title process uses cheap raw
     materials.
               THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 10
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
     Processes for the preparation of 5-hydroxy-3-oxopentanoic acid derivatives
     2000:881110 CAPLUS
     134:41920
     Processes for the preparation of 5-hydroxy-3-oxopentanoic acid derivatives
     Nishiyama, Akira; Inoue, Kenji
     Kaneka Corp., Japan
     PCT Int. Appl., 32 pp.
     CODEN: PIXXD2
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FAN.CNT 2
                        KIND DATE
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JP 2000-23804 A 20000201

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                     KIND DATE
                                          APPLICATION NO. DATE
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                                          WO 1999-JP4229 19990805
    WO 2000008011
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                                                            20020913
                            20030227
     US 2003040634
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                                           JP 1998-221495 A 19980805
                                           JP 1999-158033 A 19990604
                                           WO 1999-JP4229 W 19990805
                                           US 2000-509998 A320000816
     CASREACT 134:41920; MARPAT 134:41920
OS
     Processes by which 5-hydroxy-3-oxopentanoic acid derivs. represented by
     formula R2CH(OH)CH2COCH2CO2R1 [I; R1 = C1-12 alkyl, C6-12 aryl, C7-12
     aralkyl; R2 = H, (un) substituted C1-12 alkyl, C2-12 alkenyl, C6-12 aryl,
     or C7-12 aralkyl, cyano, CO2H, alkoxycarbonyl], useful as intermediates of
     drugs, in particular HMG-CoA reductase inhibitors, can be prepared from
     inexpensive and easily available raw materials under noncryogenic
     conditions. Specifically, described are a process for preparing
     5-hydroxy-3-oxopentanoic acid derivs. I by making lithium amide act on a
     mixture of an acetic acid ester and a 3-hydroxypropionic acid derivative at a
     temperature of -20\,^{\circ}\text{C} or above; and another process for preparing
     5-hydroxy-3-oxopentanoic acid derivs. by treating a mixture of an acetic
     acid ester and a 3-hydroxypropionic acid derivative with a Grignard reagent
```

and then making lithium amide act on the resulting mixture at a temperature of -20° or above. These processes are carried under moderately low temperature compared to known methods which require very cold temperature (-78° to -40°). Thus, a solution of 3.90 g diisopropylamine in 3 mL THF was added dropwise to 22.9 mL 1.5 mol/L BuLi/hexane with stirring at 5° and stirred fro 1 h to give a solution of lithium diisopropylamide. Tert-butylmagnesium chloride/PhMe-THF (1:2.5) (1.75 mol/kg, 5.7 g) was added to a solution of 2.38 g Et 4-benzyloxy-3-hydroxybutyrate and 2.32 g tert-Bu acetate in 3.0 mL THF with stirring at 0-5° over a period of 10 min and stirred at 5° for 50 min, followed by adding dropwise the lithium diisopropylamide solution prepared above over a period of 30 min, and the resulting mixture was stirred at 5-20° for 16 h and poured into a mixture of 3 N aqueous HCl and 30 mL EtOAc to give, after workup and silica gel chromatog., 79% 6-benzyloxy-5-hydroxy-3-oxohexanoic acid tert-Bu ester.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
L10
     Process for the preparation of optically active 2-[6-(hydroxymethyl)-1,3-
TI
     dioxan-4-yl]acetic acid derivatives
     2000:117041 CAPLUS
AN
     132:166230
DN
     Process for the preparation of optically active 2-[6-(hydroxymethyl)-1,3-
TΤ
     dioxan-4-yl]acetic acid derivatives
     Kizaki, Noriyuki; Yamada, Yukio; Yasohara, Yoshihiko; Nishiyama, Akira;
TN
     Miyazaki, Makoto; Mitsuda, Masaru; Kondo, Takeshi; Ueyama, Noboru; Inoue,
     Kenji
PA
     Kaneka Corporation, Japan
     PCT Int. Appl., 64 pp.
SO
     CODEN: PIXXD2
ידת
     Patent
     Japanese
LΑ
FAN.CNT 2
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                      KIND DATE
                     A1 20000217
                                                            19990805
     WO 2000008011
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20021029

В1

US 6472544

WO 1999-JP4229 W 19990805

20000816

US 2000-509998

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JP 1998-221495 A 19980805
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     US 2003040634
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                                 20030227
                                                  US 2002-242453
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FAN 2000:881110
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                                                  APPLICATION NO. DATE
     WO 2000075099
                                                 WO 2000-JP3574 20000602
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                                20001214
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               SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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                                                   JP 1999-158033 A 19990604
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      CASREACT 132:166230; MARPAT 132:166230
OS
GΙ
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R4 R5 O O CO2R1 III
$$\times^1$$
 CO2R1 III \times^1 CO2R1 \times^1 \times^1 CO2R1 \times^1 \times^1

Described is a process for the preparation of optically active AΒ 2-[6-(hydroxymethyl)-1,3-dioxan-4-yl] acetic acid derivs. (I; R = H; R1 = H, C1-12 alkyl, C6-12 aryl, C7-12 aralkyl; R4, R5 = H, C1-12 alkyl, C6-12aryl, C7-12 aralkyl; or R4 and R5 are linked together to form a ring), which comprises subjecting an enolate prepared by reacting an acetate ester derivative X2CH2CO2R1 (X2 = H, halo; R1 = same as above) with either a base or a zero-valent metal to reaction with a hydroxybutyric acid derivative (II; X1 = halo; R2 = same as above) at -30° or above to thereby obtain a hydroxyoxohexanoic acid derivative (III; R1, X1 = same as above), reducing this hydroxyoxohexanoic acid derivative with a microorganism into a dihydroxyhexanoic acid derivative (IV; R1, X1 = same as above), treating this dihydroxyhexanoic acid derivative with an acetal-forming reactant in the presence of an acid to thereby obtain a halomethyldioxanylacetic acid derivative (V; X1, R1, R4 , R5 = same as above), acyloxylating this halomethyldioxanylacetic acid derivative with an acyloxylating agent into an acyloxymethyldioxanylacetic acid derivative I (R = R3CO; R3 = H, C1-12 alkyl, C6-12 aryl, C7-12 aralkyl), and subjecting this acyloxymethyldioxanylacetic acid derivative to solvolysis in the presence of a base. Thus, a solution of tert-butylmagnesium chloride in PhMe/THF was added dropwise over 30 min to a THF solution of Et (3S)-4-chloro-3-hydroxybutyrate and tert-Bu acetate with stirring at 0-5° and stirred at 5° for 30 min, followed by adding dropwise a freshly prepared solution of lithium diisopropylamide in THF at 5° for 30 min, and the resulting mixture was stirred at 5° for 16 h to give 78% (5S)-6-chloro-5-hydroxy-3oxohexanoic acid tert-Bu ester. A 1% solution of the latter ketone ester in 50 mM phosphate buffer (pH 6.5) containing 2% glucose was mixed with a cultured broth of Candida magnoliae and subjected to microbial reduction at 30° for 20 h to give 71% (3R,5S)-6-chloro-3,5-dihydroxyhexanoic acid tert-Bu ester (100% e.e.). The latter compound was dissolved in acetone, followed by adding 2,2-dimethoxypropane and p-MeC6H4SO3H, and the resulting mixture was stirred at room temperature for 4.5 h to give 99% 2-[(4R,6S)-6-(chloromethyl)-2,2-dimethyl-1,3-dioxan-4-yl]acetic acid tert-Bu ester which was stirred with KOAc in DMF at 100° for 20 h to give 81% 2-[(4R,6S)-6-(acetoxymethyl)-2,2-dimethyl-1,3-dioxan-4yl]acetic acid tert-Bu ester. The latter compound was dissolved in MeOH and stirred with K2CO3 under ice-cooling for 4 h to give 100% 2-[(4R,6S)-6-(hydroxymethyl)-2,2-dimethyl-1,3-dioxan-4-yl]acetic acid tert-Bu ester.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Isoquinolone derivatives, their production and use

AN 1991:514373 CAPLUS

DN 115:114373

TI Isoquinolone derivatives, their production and use

IN Natsugari, Hideaki; Ikeda, Hitoshi

PA Takeda Chemical Industries, Ltd., Japan

SO Eur. Pat. Appl., 70 pp.

CODEN: EPXXDW

DT Patent LA English

FAN CNT 1

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									JP	1990-80184	19900328
	CA	2028538		A.	Ą	1991	0428		CA	1990-2028538	19901025
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									JP	1990-80184	19900328
	JΡ	03279362		A2	2	1991	1210		JP	1990-290250	19901026
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									JP	1989-280602	19891027
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OS MARPAT 115:114373

GΙ

$$^{\rm Y}$$
 $^{\rm NR}^{\rm 1}$
 $^{\rm R2}$
 $^{\rm XCH\,(OH)\,CH_2CH\,(OH)\,CH_2CO_2R}$ I

The title compds., e.g., I [R = Me, Na; X = (CH2)2, CH:CH, Y = O, S; R1, R2 = H, alkyl, azolyl; R3 = H, Me, Cl, F, MeO], II, and their tetrahydro derivs., e.g., III were prepared from benzopyranones, e.g., IV (Ar = substituted Ph) and tested as inhibitor of the 3-hydroxy-3-Me CoA

(HMG-CoA) reductase. I and II are more active than mevinolin as HMG-CoA inhibitors, thus disrupting the biosynthesis of cholesterol.

```
L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
     Preparation of anticholesteremic (R-(R*R*))-2-(4-fluorophenyl)-\beta,
TI
     \delta-dihydroxy-5-(1-methylethyl-3-phenyl-4((phenylamino)carbonyl)-1H-
     pyrrolyl-1-heptanoic acid, its lactone form and salts thereof
     1991:429107 CAPLUS
AN
     115:29107
DN
     Preparation of anticholesteremic (R-(R*R*))-2-(4-fluorophenyl)-\beta,
TI
     \delta-dihydroxy-5-(1-methylethyl-3-phenyl-4((phenylamino)carbonyl)-1H-
     pyrrolyl-1-heptanoic acid, its lactone form and salts thereof
     Roth, Bruce David
TN
     Warner-Lambert Co., USA
PΑ
SO
     Eur. Pat. Appl., 18 pp.
     CODEN: EPXXDW
DТ
     Patent
     English
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                                            APPLICATION NO. DATE
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     ES 2167306
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                                            US 1989-384187 A 19890721
                                            JP 1990-190935 A319900720
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                                                              19900723
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     US 5273995
                        Α
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                                            NO 1993-2075
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     NO 9302075
                             19910122
                        Α
                             19941024
     NO 176096
                        С
                             19950201
     NO 176096
```

US 1989-384187 A 19890721

AB Title compound, lactone derivative I, and pharmaceutically acceptable salts thereof were prepared Treatment of hydroxyketoester II (preparation given) with

II

Ι

B(Et)3, NaBH4 in MeOH, H2O2, and NaOH gave the corresponding Na dihydroxyheptanoate derivative which was converted to the acid. This acid was taken up in toluene and refluxed using a Dean-Stark trap for 20 min to give I. II exhibited IC50 of 0.0044 $\mu\text{M}/\text{L}$ against cholesterol biosynthesis.

=> logoff hold SINCE FILE TOTAL COST IN U.S. DOLLARS SESSION ENTRY 46.95 212.98 FULL ESTIMATED COST TOTAL SINCE FILE DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) ENTRY SESSION -4.16-4.16CA SUBSCRIBER PRICE

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STN INTERNATIONAL SESSION SUSPENDED AT 07:43:03 ON 16 MAR 2004

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PASSWORD:

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STRUCTURE FILE UPDATES: 15 MAR 2004 HIGHEST RN 663595-21-9 DICTIONARY FILE UPDATES: 15 MAR 2004 HIGHEST RN 663595-21-9

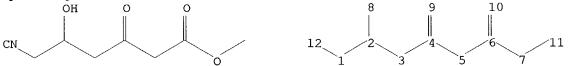
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

Uploading C:\Examination Auxillary files\10705665\10705665 product with CN.str



chain nodes :

1 2 3 4 5 6 7 8 9 10 11 12

chain bonds :

1-2 1-12 2-3 2-8 3-4 4-5 4-9 5-6 6-7 6-10 7-11

exact/norm bonds :

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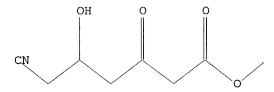
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L11 STRUCTURE UPLOADED

=> d 111

L11 HAS NO ANSWERS

L11 STR



Structure attributes must be viewed using STN Express query preparation.

=> search 111 sss sam

SAMPLE SEARCH INITIATED 07:58:21 FILE 'REGISTRY'

COMMAND INTERRUPTED

If this message appears repeatedly, please notify the Help Desk. Enter "HELP STN" for information on contacting the nearest STN Help Desk by telephone or via SEND in the STNMAIL file.

=> search lll sss sam

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100.0% PROCESSED 44 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 483 TO 1277

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=> search lll sss full

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FULL SCREEN SEARCH COMPLETED - 746 TO ITERATE

100.0% PROCESSED 746 ITERATIONS 2 ANSWERS

SEARCH TIME: 00.00.01

L13 2 SEA SSS FUL L11

=> d scan

L13 2 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Hexanoic acid, 6-cyano-5-hydroxy-3-oxo-, 1,1-dimethylethyl ester, (5R)-

(9CI) MF C11 H17 N O4

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L13 2 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN

IN Hexanoic acid, 6-cyano-5-hydroxy-3-oxo-, 1,1-dimethylethyl ester, (5S)-(9CI)

MF C11 H17 N O4

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus SINCE FILE TOTAL COST IN U.S. DOLLARS ENTRY SESSION 155.84 371.01 FULL ESTIMATED COST SINCE FILE TOTAL DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) ENTRY SESSION 0.00 -4.16CA SUBSCRIBER PRICE

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FILE COVERS 1907 - 16 Mar 2004 VOL 140 ISS 12

FILE LAST UPDATED: 15 Mar 2004 (20040315/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> 113

L14 9 L13

=> d 114 1-9 ti

- L14 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- Process for the preparation of 7-amino-syn-3,5-dihydroxyheptanoic acid derivatives via 6-cyano-syn-3,5-dihydroxyhexanoic acid derivatives as intermediates used in the preparation of statin derivatives
- L14 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Process for producing optically pure δ -hydroxy- β -keto ester derivatives
- L14 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Processes for the preparation of 5-hydroxy-3-oxopentanoic acid derivatives
- L14 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Preparation of cis-1,3-diols from β hydroxy ketones using a trialkylborane and/or dialkylalkoxyborane
- L14 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Process for the synthesis of protected esters of (s)-3,4-dihydroxybutyric acid
- L14 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Reduction of ketone groups
- L14 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Process for the synthesis of (5R)-1,1-dimethylethyl 6-cyano-5-hydroxy-3-oxohexanoate
- L14 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI The synthesis of (4R-cis)-1,1-dimethylethyl 6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate, a key intermediate for the preparation of CI-981, a high potent, tissue selective inhibitor of HMG-CoA reductase
- L14 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Improved process for trans-6-(pyrroloethyl)pyran-2-one inhibitors of cholesterol synthesis

=> d 114 9 ti fbib abs

- L14 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Improved process for trans-6-(pyrroloethyl)pyran-2-one inhibitors of cholesterol synthesis
- AN 1990:216691 CAPLUS
- DN 112:216691
- TI Improved process for trans-6-(pyrroloethyl)pyran-2-one inhibitors of cholesterol synthesis
- IN Butler, Donald Eugene; Deering, Carl Francis; Millar, Alan; Nanninga, Thomas Norman; Roth, Bruce David
- PA Warner-Lambert Co., USA
- SO PCT Int. Appl., 120 pp. CODEN: PIXXD2
- DT Patent

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		94958 94958		B C	19950815 19951127		FI 1990-4118 19900820
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ГТ	93958	C	19930020	пс	1988-158439	Δ	19880222	
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NO 9603245	Α	19900927	NO 1996-3245 19960802
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KR 137884	В1	19980501	KR 1997-702620 19970421
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JP 10195071	A2	19980728	JP 1998-22559 19980121
JP 3009139	B2	20000214	
			US 1988-158439 A 19880222
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			JP 1989-503113 A319890222
MADDAT 112.21660	1 1		

os MARPAT 112:216691

GΙ

R2
R2
N(CH₂)₂

$$R^{1}$$
 R^{2}
 R^{3}
 R^{4}
 R^{7}
 R^{8}
 R^{8}
 R^{5}
 R^{2}
 R^{1}
 R^{7}
 R^{8}
 R^{8}
 R^{1}
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 R^{4}
 R^{4}

Title compds. I [R1 = (substituted) Ph, 1- or 2-naphthyl, cyclohexyl (methyl), pyridyl, etc.; R2, R3 = H, alkyl, cycloalkyl, (substituted) Ph, etc.; R4 = alkyl, cycloalkyl, CF3], useful as cholesterol synthesis inhibitors (no data), are prepared from (H2C:CHCH2)2CHOH via an epoxide II, dioxanes III [R5 = cyano; R6 = CH:CH2; R7, R8 = H, alkyl, Ph, R7R8 = (CH2)n; n = 4, 5], III (R6 = CH0), III (R6 = CO2H), III (R6 = CO2R9; R9 = alkyl, cycloalkyl), III (R5 = CH2NH2), and III [R5 = QCH2; R6 = CO2R9; R7, R8 = H, alkyl, Ph; R7R8 = (CH2)n; n = 4, 5], resp. A solution of III (R5 = CH2NH2; R6 = CO2CHMe2; R7 = R8 = Me) and 4-FC6H4CO(CH2)2COEt (preparation given) in PhMe was refluxed to give III (R5 = QCH2; R1 = Et; R2 = R3 = H; R4 = 4-FC6H4), which was successively treated with HCl/THF and aqueous NaOH (pH 10), and the product in PhMe was refluxed with azeotropic removal of H2O to give I (R1 = Et; R2 = R3 = H; R4 = 4-FC6H4).

=> d 114 7 ti fbib abs

L14 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

TI Process for the synthesis of (5R)-1,1-dimethylethyl 6-cyano-5-hydroxy-3-oxohexanoate

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AN
     1993:41188 CAPLUS
DN
     118:41188
     Process for the synthesis of (5R)-1,1-dimethylethyl 6-cyano-5-hydroxy-3-
ΤI
     oxohexanoate
     Butler, Donald E.; Le, Tung V.; Millar, Alan; Nanninga, Thomas N.
ΤN
     Warner-Lambert Co., USA
PA
SO
     U.S., 8 pp.
     CODEN: USXXAM
DΤ
     Patent
     English
LА
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO.
                                                            DATE
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                                                             19911011
PΤ
     US 5155251
                      Α
                            19921013
                                           US 1991-775162
                                           WO 1992-US8441
                                                            19921005
     WO 9307115
                      A1
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         W: AU, CA, CS, FI, HU, JP, KR, NO, RU
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE
                                           US 1991-775162 A 19911011
                                           AU 1992-27641
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     AU 9227641
                       A1
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     AU 667320
                       В2
                            19960321
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                                           WO 1992-US8441 A 19921005
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                       T2
                            19950105
                                           JP 1992-507100 19921005
                                           US 1991-775162 A 19911011
                                           WO 1992-US8441 W 19921005
                            19950322
                                           EP 1992-921435
                                                             19921005
     EP 643689
                       A1
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                            19981230
                       B1.
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE
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                                           WO 1992-US8441 W 19921005
     AT 175190
                       Ε
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                                           AT 1992-921435
                                                            19921005
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                                           ES 1992-921435
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     ES 2129457
                       Т3
                                           US 1991-775162 A 19911011
                            20011225
                                           JP 1993-507100 19921005
     JP 3241723
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                                           US 1991-775162 A 19911011
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     ZA 9207793
                            19940411
                                           ZA 1992-7793
                                                            19921009
                       Α
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                                           FI 1994-1632
                                                             19940408
                       Α
                                           US 1991-775162 A 19911011
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     NO 9401280
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                                           NO 1994-1280
                                                             19940408
                       Α
                                           US 1991-775162 A 19911011
                                           WO 1992-US8441 A 19921005
OS
     MARPAT 118:41188
AΒ
     Title compound (I), difficult to produce on a large scale by prior art, is
     prepared by an improved, short, efficient, an economical process, by
     reaction of the anion of tert-Bu acetate with (3R)-4-cyano-3-
     hydroxybutyric acid esters. I is an intermediate in preparation of
     (2R-trans)-5-(4-fluorophenyl)-2-(1-methylethyl)-N,4-diphenyl-1-[2-
     (tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamode
     (II) which is an inhibitor of cholesterol acyltransferase. NaCN in H2O
     was added to (S)-BrCH2CH(OH)CH2CO2Et, the reaction stirred for 16 h at
     room temperature to give Et (R)-NCCH2CH(OH)CH2CO2Et (III). To (Me2CH)2NLi in
     THF was added Me3COAc followed by THF, the mixture stirred and added to III
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in THF to give I. I was converted in 5 steps to II.

9 L13 3121986 PREP/RL 7 L13/PREP

(L13 (L) PREP/RL)

=> d 115 1-7 ti fbib abs

L15 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

Process for the preparation of 7-amino-syn-3,5-dihydroxyheptanoic acid derivatives via 6-cyano-syn-3,5-dihydroxyhexanoic acid derivatives as intermediates used in the preparation of statin derivatives

AN 2003:42235 CAPLUS

DN 138:89624

L15

Process for the preparation of 7-amino-syn-3,5-dihydroxyheptanoic acid derivatives via 6-cyano-syn-3,5-dihydroxyhexanoic acid derivatives as intermediates used in the preparation of statin derivatives

IN Oehrlein, Reinhold; Baisch, Gabriele; Kirner, Hans Joerg; Bienewald, Frank; Burkhardt, Stephan; Studer, Martin

PA Ciba Specialty Chemicals Holding Inc., Switz.

SO PCT Int. Appl., 38 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

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PATENT NO.
                       KIND DATE
                                             APPLICATION NO. DATE
                             _____
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                      ____
                       A1 20030116
                                       WO 2002-EP7309 20020702
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     WO 2003004456
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
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              CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
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EP 2001-810670 A 20010706

PATENT FAMILY INFORMATION:

FAN 2003:42229

	PAT	CENT 1	NO.		KI	ND 1	DATE			A.	PPLI	CATI	ои ис	٥.	DATE			
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			ТJ,	TM														
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			PT,	SE,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,
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EP 2001-810670 A 20010706

FAN 2003:42234

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	WO 2003004455	A2	20030116	WO 2002-EP7308	20020702
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             NE, SN, TD, TG
                                              EP 2001-810670 A 20010706
    MARPAT 138:89624
     OR?
          OR?
        Ι
     The invention relates to novel methods for the synthesis of intermediates,
     especially 7-amino-3,5-dihydroxyheptanoic acid derivs. I [R = H2NCH2, NC; Ra,
     = H or a hydroxy-protecting group or together are a bridging
     hydroxy-protecting group; Rc is a carboxy-protecting group], which are
     suitable for the preparation of statin derivs. Thus, (3R)-acetoxyglutaric acid
     monoethyl ester monoamide was prepared from di-Et 3-hydroxyglutaric acid and
     reacted with cyanuric chloride to give (R)-NCCH2CH(OAc)CH2CO2Et, which is
     an intermediate in the preparation of title derivs. and atorvastatin.
               THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 12
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
     Process for producing optically pure \delta-hydroxy-\beta-keto ester
     derivatives
     2002:927437 CAPLUS
     138:13919
     Process for producing optically pure \delta-hydroxy-\beta-keto ester
     derivatives
     Cho, Yik-Haeng; Roh, Kyoung Rok; Shin, Jong Hyun; Chun, Jong Pil; Yu, Ho
     Sung; Cho, Chang-Woo
     Samsung Fine Chemicals Co., Ltd., S. Korea
     PCT Int. Appl., 41 pp.
     CODEN: PIXXD2
     Patent
     English
FAN.CNT 1
                              DATE
                                              APPLICATION NO. DATE
     PATENT NO.
                       KIND
                              20021205
                                                                20011121
                                             WO 2001-KR2003
     WO 2002096915
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              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS,
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              UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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              BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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KR 2001-28984 A 20010525

OS GΙ

AB

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L15

AN

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PA

SO

DT

LΑ

PI

OS

Optically pure δ -hydroxy- β -keto esters I [R1 = halogen, CN, OH, protected OH; R2 = H, protective group; R3 = alkyl, CH2Ph] were prepared by treating an imidazolide II with Meldrum's acid under mild conditions in the presence of a base to produce an acyl-Meldrum's acid III, and heating this at reflux in an alc. to obtain optically pure I. Thus, (R)-NCCH2CH(OSiMe2CMe3)CH2CO2H, prepared from (S)-3-hydroxy- γ -butyrolactone in 5 steps, was converted to its imidazolide, treated with Meldrum's acid in presence of pyridine and solvolyzed with Me3COH to give I [R1 = CN, R2 = SiMe2CMe3, R3 = CMe3]. This acid was desilylated and converted to its 3,5-di-O-isopropylidene derivative I are useful as synthetic intermediates.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L15 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
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TI Processes for the preparation of 5-hydroxy-3-oxopentanoic acid derivatives

AN 2000:881110 CAPLUS

DN 134:41920

TI Processes for the preparation of 5-hydroxy-3-oxopentanoic acid derivatives

IN Nishiyama, Akira; Inoue, Kenji

PA Kaneka Corp., Japan

SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

DATE PATENT NO. KIND DATE APPLICATION NO. _____ 20000602 WO 2000075099 WO 2000-JP3574 20001214 A1 PΙ W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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                                          JP 1999-158033 A 19990604
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                                          WO 2000-JP3574 W 20000602
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                                          WO 2000-JP3574 W 20000602
PATENT FAMILY INFORMATION:
FAN 2000:117041
                     KIND DATE
                                         APPLICATION NO. DATE
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                     A1 20000217
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            PT, SE
                                          JP 1998-221495 A 19980805
                                          JP 1999-158033 A 19990604
    CA 2305564
                      AΑ
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                                          CA 1999-2305564 19990805
                                          JP 1998-221495 A 19980805
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                                          WO 1999-JP4229 W 19990805
                                          EP 1999-935066 19990805
                      A1 20000802
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        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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                     A2 20040303
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    EP 1394157
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            IE, SI, LT, LV, FI, RO, MK, CY, AL
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                           20000403
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                                          JP 1998-221495 A 19980805
                                          JP 1999-158033 A 19990604
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                                                          20000816
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    US 6472544
                                          JP 1998-221495 A 19980805
                                          JP 1999-158033 A 19990604
                                          WO 1999-JP4229 W 19990805
                           20030227
                                          US 2002-242453 20020913
    US 2003040634
                   A1
                                          JP 1998-221495 A 19980805
                                          JP 1999-158033 A 19990604
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OS CASREACT 134:41920; MARPAT 134:41920

Processes by which 5-hydroxy-3-oxopentanoic acid derivs. represented by AΒ formula R2CH(OH)CH2COCH2CO2R1 [I; R1 = C1-12 alkyl, C6-12 aryl, C7-12 aralkyl; R2 = H, (un) substituted C1-12 alkyl, C2-12 alkenyl, C6-12 aryl, or C7-12 aralkyl, cyano, CO2H, alkoxycarbonyl], useful as intermediates of drugs, in particular HMG-CoA reductase inhibitors, can be prepared from inexpensive and easily available raw materials under noncryogenic conditions. Specifically, described are a process for preparing 5-hydroxy-3-oxopentanoic acid derivs. I by making lithium amide act on a mixture of an acetic acid ester and a 3-hydroxypropionic acid derivative at a temperature of -20°C or above; and another process for preparing 5-hydroxy-3-oxopentanoic acid derivs. by treating a mixture of an acetic acid ester and a 3-hydroxypropionic acid derivative with a Grignard reagent and then making lithium amide act on the resulting mixture at a temperature of -20° or above. These processes are carried under moderately low temperature compared to known methods which require very cold temperature (-78° to -40°). Thus, a solution of 3.90 g diisopropylamine in 3 mL THF was added dropwise to 22.9 mL 1.5 mol/L BuLi/hexane with stirring at 5 and stirred fro 1 h to give a solution of lithium diisopropylamide. Tert-butylmagnesium chloride/PhMe-THF (1:2.5) (1.75 mol/kg, 5.7 g) was added to a solution of 2.38 g Et 4-benzyloxy-3-hydroxybutyrate and 2.32 g tert-Bu acetate in 3.0 mL THF with stirring at 0-5° over a period of 10 min and stirred at 5° for 50 min, followed by adding dropwise the lithium diisopropylamide solution prepared above over a period of 30 min, and the resulting mixture was stirred at 5-20° for 16 h and poured into a mixture of 3 N aqueous HCl and 30 mL EtOAc to give, after workup and silica gel chromatog., 79% 6-benzyloxy-5-hydroxy-3-oxohexanoic acid tert-Bu ester.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of cis-1,3-diols from β hydroxy ketones using a trialkylborane and/or dialkylalkoxyborane

AN 1999:421640 CAPLUS

DN 131:60318

TI Preparation of cis-1,3-diols from β hydroxy ketones using a trialkylborane and/or dialkylalkoxyborane

IN McCabe, Richard Joseph; Nanninga, Thomas Norman; Bosch, Robert Lee; Stahl, Robert Joseph

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PAN.	PATENT NO.	KIND DATE	1	APPLICATION NO. DATE
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		MD, RU, TJ, TM		
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	,			US 1997-68193P P 19971219
	CA 2305618	AA 1999	0701	CA 1998-2305618 19981202
				US 1997-68193P P 19971219
				WO 1998-US25493W 19981202
	AU 9917074	A1 1999	0712	AU 1999-17074 19981202

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AU 755543
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                                      US 1997-68193P P 19971219
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BR 9813760
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                       20001003
                                       BR 1998-13760
                                      US 1997-68193P P 19971219
                                      WO 1998-US25493W 19981202
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                                       WO 1998-US25493W 19981202
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TW 444000
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                                       US 1997-68193P P 19971219
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US 6433213
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                       20021031
                                       US 2002-166990
                                                        20020611
US 2002161021
                  A1
US 6596879
                  В2
                        20030722
                                       US 1997-68193P P 19971219
                                       WO 1998-US25493W 19981202
                                       US 2000-581798 A320000616
US 2004006231
                  A1
                       20040108
                                       US 2003-411886
                                                        20030411
                                       US 1997-68193P P 19971219
                                       WO 1998-US25493W 19981202
                                       US 2000-581798 A320000616
                                       US 2002-166990 A320020611
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OS MARPAT 131:60318

AB Cis-1,3-diols RCH(OH)CH2CH(OH)R1, where R = alkyl, NCCH2, PG-OCH2; PG is a protecting group; R1 = alkyl, CH2CO2R6; R6 = alkyl; useful as intermediates in preparation of HMG CoA reductase inhibitors (no data), are prepared by treating a β-hydroxyketone with a trialkylborane and/or dialkylalkoxyborane in a solvent, then with an alkali metal hydride, followed by recovery and reuse of the alkylborane species. Using a minimal amount of acid in the reduction and workup and keeping the distillate streams sep. allows recovery and reuse of the alkylboranes, which act synergistically when used together. Thus, crude [R-(R*,R*)]-1,1-dimethylethyl 6-cyano-3,5-dihydroxyhexanoate was prepared from crude 5R 1,1-dimethylethyl 6-cyano-5-hydroxy-3-oxohexanoate using .apprx.4:1 triethylborane and diethylmethoxyborane and converted to (4R cis) 1,1-dimethylethyl 6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate showing cis:trans ratio >50:1.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L15 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Process for the synthesis of protected esters of (s)-3,4-dihydroxybutyric acid
- AN 1998:102860 CAPLUS
- DN 128:154074
- TI Process for the synthesis of protected esters of (s)-3,4-dihydroxybutyric acid
- IN Jacks, Thomas Elliott; Butler, Donald Eugene

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Warner-Lambert Company, USA; Jacks, Thomas Elliott; Butler, Donald Eugene
PA
SO
     PCT Int. Appl., 40 pp.
     CODEN: PIXXD2
     Patent
DT
     English
LA
FAN.CNT 1
                                              APPLICATION NO. DATE
     PATENT NO.
                        KIND DATE
                                               _____
                                              WO 1997-US11654 19970701
                              19980205
                       A1
     WO 9804543
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                                               US 1996-22369P P 19960729
                                               AU 1997-35154
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                         A1,
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                                               нк 1999-105756
                                                                  19991209
      HK 1020728
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                                               US 1996-22369P P 19960729
                                               WO 1997-US11654W 19970701
      CASREACT 128:154074; MARPAT 128:154074
OS
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GΙ

AB The title compds. (I; R, R1 = C1-3 alkyl; R2 = C1-8 alkyl) are prepared in a one pot process from a carbohydrate substrate. The process comprises (a) treating a carbohydrate substrate with H2O2 in the presence of base and

subsequent acidification with an acid; (b) cyclization; (c) esterification; (d) protecting the diol.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L15 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
- TI Process for the synthesis of (5R)-1,1-dimethylethyl 6-cyano-5-hydroxy-3-oxohexanoate
- AN 1993:41188 CAPLUS
- DN 118:41188
- TI Process for the synthesis of (5R)-1,1-dimethylethyl 6-cyano-5-hydroxy-3-oxohexanoate
- IN Butler, Donald E.; Le, Tung V.; Millar, Alan; Nanninga, Thomas N.
- PA Warner-Lambert Co., USA
- SO U.S., 8 pp. CODEN: USXXAM
- DT Patent
- LA English
- FAN. CNT 1

FAN.	PAT	TENT NO.				APPLICATION NO.	DATE	
PI	US	5155251	Α	19921013		US 1991-775162	19911011	
	WO	930/115 W: AU, CA,				WO 1992-US8441	19921003	
		RW: AU, CA,	CH. DE.	DK. ES.	FR.	GB, GR, IE, IT, LU	, MC, NL,	SE
		100. THY DD,	011, 021	, 211, _22,	,	US 1991-775162 A	19911011	
	AU	9227641	A1	19930503		AU 1992-27641		
	AU	667320	В2	19960321				
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						WO 1992-US8441 A	19921005	
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	EΡ	643689	A1	19950322		EP 1992-921435	19921005	
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		R: AT, BE,	CH, DE	, DK, ES,	FR,	GB, GR, IE, IT, LI		NL, SE
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						WO 1992-US8441 W		
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						US 1991-775162 A		
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						JP 1993-507100 A		
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			_			US 1991-775162 A		
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						US 1991-775162 A		
		0.407.000		10040400		WO 1992-US8441 W		
	ИО	9401280	Α	19940408				
						US 1991-775162 A	. 19911011	

OS MARPAT 118:41188

Title compound (I), difficult to produce on a large scale by prior art, is prepared by an improved, short, efficient, an economical process, by reaction of the anion of tert-Bu acetate with (3R)-4-cyano-3-hydroxybutyric acid esters. I is an intermediate in preparation of (2R-trans)-5-(4-fluorophenyl)-2-(1-methylethyl)-N,4-diphenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamode

WO 1992-US8441 A 19921005

(II) which is an inhibitor of cholesterol acyltransferase. NaCN in H2O was added to (S)-BrCH2CH(OH)CH2CO2Et, the reaction stirred for 16 h at room temperature to give Et (R)-NCCH2CH(OH)CH2CO2Et (III). To (Me2CH)2NLi in THF was added Me3COAc followed by THF, the mixture stirred and added to III in THF to give I. I was converted in 5 steps to II.

L15 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

TI The synthesis of (4R-cis)-1,1-dimethylethyl 6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate, a key intermediate for the preparation of CI-981, a high potent, tissue selective inhibitor of HMG-CoA reductase

AN 1992:426454 CAPLUS

DN 117:26454

TI The synthesis of (4R-cis)-1,1-dimethylethyl 6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate, a key intermediate for the preparation of CI-981, a high potent, tissue selective inhibitor of HMG-CoA reductase

AU Brower, Philip L.; Butler, Donald E.; Deering, Carl F.; Le, Tung V.; Millar, Alan; Nanninga, Thomas N.; Roth, Bruce D.

CS Parke-Davis Pharm. Res. Div., Warner Lambert Co., Holland, MI, 49424, USA

SO Tetrahedron Letters (1992), 33(17), 2279-82 CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA English

OS CASREACT 117:26454

GΙ

AB Three alternative methods for the synthesis of the optically active heptanoate I, a key intermediate in the preparation of a highly potent and tissue selective HMG Co-A reductase inhibitor are described. Thus, NCCH2CH(OH)CH2CO2R (R = Me, Et, Bu) underwent a cross Claisen using lithium tert-Bu acetate to give I in 65-70% yields.

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FULL ESTIMATED COST	50.19	421.20
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CA SUBSCRIBER PRICE	-6.24	-10.40

SESSION WILL BE HELD FOR 60 MINUTES
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Connecting via Winsock to STN

Welcome to STN International! Enter x:x

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Connecting via Winsock to STN

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=> d his

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